UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,596	05/03/2002	Audrey Goddard	P3230R1C001-168	2711

20995 7590 07/25/2006

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,596	GODDARD ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *5/3/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/9/06,4/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

The information disclosure statement submitted on 9 March 2006 has been considered. The information disclosure statement submitted on 11 April 2006 have been considered. Citations crossed off by the Examiner have been cited in duplicate.

Claims 6-17 are under consideration in the instant application.

Claim Rejections/Objections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

Claims 6-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Novel biological molecules lack well-established utilities and must undergo extensive experimentation. The basis for this rejection is set forth for at p. 3-10 of the previous Office Action (9 January 2006).

Claims 6-17 are directed to an isolated polypeptide having 95- 99% amino acid sequence identity to (a) the amino acid sequence of the polypeptide of SEQ ID NO: 90, (b) the amino acid

sequence of the polypeptide of SEQ ID NO: 90, lacking its associated signal peptide, or (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203236; wherein the nucleic acid encoding the polypeptide is over-expressed in kidney tumor cells. The claims also recite a chimeric polypeptide comprising a polypeptide fused to a heterologous polypeptide.

Applicant's arguments (11 April 2006), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons:

In the Response of 11 April 2006 (p. 16), Applicant has submitted teachings from Alberts, B. (Molecular Biology of the Cell (1994) and Lewin, B. (Genes VI, 1997) to support the statements of Dr. Grimaldi (Grimaldi and Polakis' declaration, see below). Applicants also cite numerous references to emphasize that those of skill in the art would not be focusing on differences in gene expression between cancer cells and normal cells if there were no correlation between gene expression and protein expression (such as Zhigang et al., Meric et al. Orntoft et al., Wang et al., Munaut et al., etc.). Applicant asserts that changes in mRNA level generally lead to corresponding changes in the level of expressed protein. Applicant also contends that the references and the Grimaldi declaration establish that the accepted understanding in the art is that there is a reasonable correlation between changes in gene expression and the level of the encoded protein.

Applicant's arguments have been fully considered but are not found to be persuasive. While the examiner acknowledges the teachings of Alberts and Lewin, which disclose that initiation of transcription is the most common point for a cell to regulate the gene expression, it

is not the only means of regulating gene expression. For example, Alberts also teaches that there are a number of other controls that can act later in the pathway from RNA to protein to modulate the amount of protein that is made, including translational control mechanisms and mRNA degradation control mechanisms (Alberts, 1994, p. 453). Meric et al. states the following: "The fundamental principle of molecular therapeutics in cancer is to exploit the differences in gene expression between cancer cells and normal cells. [M]ost efforts have concentrated on identifying differences in gene expression at the level or mRNA, which can be attributable to either DNA amplification or to differences in transcription."

However, Meric et al. also go on to state that gene expression is quite complicated, and is also regulated at the level of mRNA stability, mRNA translation, and protein stability (see page 971 of Introduction). Meric et al. also teaches that there are a number of translation alterations encountered in cancer, including variations in the mRNA sequence as a result of mutations, alternate splicing and transcription start sites, alternate polyadenylation sites, and alterations in the components of the translation machinery (see pages 973-974). Celis et al. also teach that "[g]enes may be present, they may be mutated, but they are not necessarily transcribed. Some messengers are transcribed but not translated, and the number of mRNA copies does not necessarily reflect the number of functional protein molecules" (p. 6, col 2).

Furthermore, all of Applicant's newly cited references (with the exception of Orntoft et al.) measure mRNA, while the assay utilized in Example 18 of the instant specification is PCR. Also, with the exception of Futcher et al., all of Applicant's newly cited references are directed to the analysis of single genes, or a small group of genes, and therefore do not demonstrate

trends found across proteins in general. The studies cited by the Applicant that examine the expression of specific genes or small numbers of genes are not found persuasive in view of comprehensive studies where significantly larger numbers of transcripts and proteins were examined and which accurately describe general trends, specifically: Haynes (80 proteins examined) and Chen (165 proteins examined) (cited previously by Examiner) and Nagaraja et al. (2006), Waghray et al. (2001) and Sagynaliev et al. (2006) (described below).

With regard to the Orntoft reference, Applicants submit that Orntoft examined 40 well-resolved abundant proteins, and found significant correlation between mRNA and protein alterations (including both increases and decreases) for each gene, except one. Applicants' arguments with respect to Orntoft have been fully considered but are not found to be persuasive. Orntoft et al. appear to have looked at increased DNA content over large regions of chromosomes and compare that to mRNA and polypeptide levels from the chromosomal region. Their approach to investigating gene copy number was termed CGH. Orntoft et al. do not appear to look at gene amplification, mRNA levels and polypeptide levels from a single gene at a time. Instead, they concentrated on regions of chromosomes with strong gains of chromosomal material containing clusters of genes (p. 40). This analysis was not done for PRO1268 in the instant specification. That is, it is not clear whether or not PRO1268 is in a gene cluster in a region of a chromosome that is highly amplified. Therefore, the relevance, if any of Orntoft et al. is not clear.

Applicant also asserts that Futcher et al. (1999) conducted a study of mRNA and protein expression in yeast and report a good correlation between protein abundance, mRNA abundance, and codon bias. Applicant's arguments have been fully considered but are not found to be

persuasive. Futcher et al concludes that "[t]his validates the use of mRNA abundance as a rough predictor of protein abundance, at least for relatively abundant proteins [emphasis added]" (p. 7368, col 1). Futcher et al. also admits that Gygi et al. performed a similar study and generated similar data, but reached a different conclusion. Futcher et al. indicates that "Gygi et al. feel that mRNA abundance is a poor predictor of protein abundance" (p. 7367, col 1, 1st full paragraph).

The examiner maintains the previous argument that mRNA levels are not necessarily predictive of protein levels, and in response to Applicants' arguments, maintains that this is true even when there is a change in the mRNA level. Comprehensive studies, where significantly large numbers of transcripts and proteins were examined, report that increases in mRNA and protein samples are not correlated. Nagaraja et al. (Oncogene, 2006, 25: 2328-2338) characterized comprehensive transcript and proteomic profiles of cell lines corresponding to normal breast (MCF10A), noninvasive breast cancer (MCF7) and invasive breast cancer (MDS-MB-231 and report that "the proteomic profiles indicated altered abundance of fewer proteins as compared to transcript profiles" (see abstract), and "the comparison of transcript profiles with proteomic profiles demonstrated that altered proteins were not always represented in the microarray designated profiles and *vice versa*" (see p. 2329, first column). Nagaraja et al. further report that, "a comparative analysis of transcripts and proteins to establish a relationship between transcript changes and protein levels has not yet become routine" (see p. 2328, second column). Lastly, Nagaraja et al. report that, "as dictated by post-transcriptional regulation, protein profiles showed far fewer changes as compared to transcript profiles" (see p. 2335, first column).

Similar results were reported by Waghray et al. (Proteomics, 1:1327-1338, 2001). Waghray et al. analyzed gene expression changes induced by dihydrotestosterone (DHT) in the androgen responsive cancer line LNCaP, at both RNA and protein levels (see abstract). In this study, Waghray et al identified transcripts from 16750 genes and found 351 genes were significantly altered by DHT treatment and the RNA level, and identified 1031 proteins and found 44 protein spots that changed in intensity (either increased or decreased). Out of the 44 protein spots that changed in intensity, Waghray et al. reports that, "remarkably, for most of the proteins identified, there was no appreciable concordant change at the RNA level" (see p. 1333-1334, Table 4). Waghray et al. clearly state that, "The change in intensity for most of the affected proteins identified could not be predicted based on the level of the corresponding RNA" (see abstract).

In a review of gene expression in colorectal cancer (CRC), Sagynaliev et al. (Proteomics, 5:3066-3078, 2005) report that "it is also difficult to reproduce transcriptomics results with proteomics tools. Out of 982 genes found to be differentially expressed in human CRC by genome-wide transcriptomics technologies (Table 6a), only 177 (18%) have been confirmed using proteomics technologies" (see p. 3068).

In summary, it is clear that Nagaraja, Waghray and Sagynaliev support the Examiner's position that *changes* in mRNA expression frequently do not result in *changes* in protein expression. It is also noted that the specification of the instant application does not teach a change in mRNA level of PRO1268. The specification simply discloses a static measurement of PRO1268 PCR in kidney tumor as compared to control. There are no teachings in the specification as to the differential expression of PRO1268 mRNA in the progression of kidney

cancer or in response to different treatments of hormones (for example). Therefore, the examiner maintains that Applicant's measurement of an increase of PRO1268 DNA does not provide a specific and substantial utility for the encoded protein, or an antibody to the protein.

Lilley et al. teach that "DNA chips can contribute to the study of gene expression in response to a particular biological perturbation. However, the extrapolation that changes in transcript level will also result in corresponding changes in protein amount or activity cannot always be made" ("Proteomics" Molecular Biology in Cellular Pathology, (2003) England: John Wiley & Sons, page 351). Wildsmith et al. also disclose that the gene expression data obtained from a microarray may differ from protein expression data ("Gene Expression Analysis Using Microarrays" Molecular Biology in Cellular Pathology, (2003) England: John Wiley & Sons, pages 269-286, especially p. 283). King et al. disclose that "it has been established that mRNA levels do not necessarily correlate with protein levels" (p. 2287, 2nd full paragraph). King et al. state that it has been demonstrated that correlation between mRNA and protein abundance is less than 0.5 and that "mRNA expression studies should be accompanied by analyses at the protein level" (p. 2287, bottom of col 1 through the top of col 2; see also Bork et al., Genome Res 398-400, 2000, especially p. 398, bottom of col 3). Haynes et al. teach that "[p]rotein expression levels are not predictable from the mRNA expression levels" (p. 1863, top of left column) and "only the direct analysis of mature protein products can reveal their correct identities, their relevant state of modification and/or association and their amounts" (p. 1870, under concluding remarks). Madoz-Gurpide et al. (cited by Applicants) disclose that "[f]or most of the published studies it is unclear how well RNA levels reported correlate with protein levels" (p. 53, 1st full paragraph).

The specification of the instant application has only disclosed that the PRO1268 polynucleotide is overexpressed in kidney tumor. The specification does not indicate that the PRO1268 polypeptide has been overexpressed in the kidney tumor sample tested. Given the asserted increase in PRO1268 expression, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that an increase in mRNA expression would correlate with significantly increased polypeptide levels. Further research needs to be done to determine whether the purported increase in PRO1268 DNA supports a role for the peptide in the cancerous tissue; such a role has not been suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in Brenner v. Manson, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,
>
> "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the specification's assertions that the PRO1268 polypeptides have utility in the fields of cancer diagnostics is not substantial.

It is noted that at pages 7-11 of the Response submitted 11 April 2006 , Applicant cites pertinent case law reviewing the legal standard of utility and the Utility Examination Guidelines. The Examiner takes no issue with Applicant's general comments regarding the legal standard for utility.

Applicant maintains that the specification at, for example, Example 18, provides sufficient disclosure to establish a specific, substantial and credible utility for the PRO1268 polypeptides. Applicant argues that Example 18 discloses that PRO1268 is significantly overexpressed in various human tumor tissues as compared to a non-cancerous human tissue control. Applicant indicates that the example explicitly states that PRO1268 is significantly overexpressed in kidney tumor as compared to normal control. Applicant argues that the utilities of PRO1268 polypeptide include its use as a diagnostic tool.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, in the instant case, the specification indicates overexpression of PRO1268 mRNA in kidney tumor tissue (the numerical increase is not known). However, the specification fails to precisely disclose any correlation between the reported overexpression of PRO1268 mRNA and PRO1268 protein expression, and more importantly, to what extent PRO1268 mRNA is reliably overexpressed in a particular tumor sample, such as kidney, such that the PRO1268 polypeptide encoded thereby could be used as a diagnostic marker for kidney tumors. There is no evidence regarding whether or not PRO1268 polypeptide levels are overexpressed in kidney tumors.

Applicant argues at p. 7 of the Response of 11 April 2006 that Feroze-Merzoug et al. (cited previously) are focusing on "accurately predicting" the precise levels of protein expression, which is not required for utility as a cancer diagnostic. Applicant states that Feroze-Merzoug et al. looked at androgen regulated genes, which were not necessarily associated with cancer. Applicant indicates that even if the teaching of Feroze-Merzoug et al. accurately reflects the correlation between mRNA and protein for the particular system studied, it does not apply to the kidney cancer diagnostic assays of the present application.

Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner is unable to locate where the Feroze-Merzoug et al. reference discusses "accurately predicting" the precise levels of protein expression. Applicant has not specifically pointed out this teaching in the reference. The Examiner is also unable to locate where Feroze-Merzoug et al. refers to Haynes et al. (as indicated by Applicant). Secondly, Feroze-Merzoug et al. reviews recent mRNA and protein expression profiling studies performed in prostate cancer. The reference discloses that "downstream genes in the androgen pathway play a critical role in the development of hormone-refractory prostate cancer" (p. 166, col 1, 1st paragraph). Thus, even though Feroze-Merzoug et al. do not examine the expression of PRO1268 of the instant application, the teachings of Feroze-Merzoug et al. clearly indicate that mRNA levels do not predict protein levels. For example, Feroze-Merzoug et al. disclose that "there is evidence highlighting the disparity between mRNA transcript and protein expression levels" and that "it will be necessary to profile both mRNA and protein for a complete picture of how cells are altered during malignant transformation" (p. 168, col 1, 1st full paragraph).

Applicant's arguments have been fully considered but are not found to be persuasive. One skilled in the art cannot determine if the "overexpression" of PRO1268 in Example 18 of the instant specification is statistically significant because of the lack of qualitative or numerical results. There is no guidance in the specification as to how high the levels of overexpression are. If a clinician took a kidney tissue sample from a patient with suspected kidney cancer, what is the likelihood that when compared with normal tissue, the level of PRO1268 from the patient would be higher? How many samples would be needed? What sensitivity would be needed? Would the normal tissue have to be a pooled sample or could it be from a single individual? Applicant has provided no indication of the nature or number of samples that were used. The only thing Applicants teach is that PRO1268 was "more highly expressed." This does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any known diseases. The specification also does not disclose at what stage of differentiation the kidney cancer sample was at or if the finding can be generalized to all kidney tumors. As was stated above (and in Hu et al. and Chen et al.), the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. Without more specifics about necessary sample size, expression level range for normal and tumor tissues, the specification has not provided the invention in a form readily usable by the skilled artisan such that significant further experimentation is unnecessary.

At p. 11-13 of the Response of 11 April 2006, Applicant argues that the Hu et al. reference (cited by examiner previously) reports flawed statistical analyses using literature mining and, as such, do not support lack of utility.

Applicant's arguments have been fully considered but are not found to be persuasive because Hu et al. provides conclusions based on many research efforts. If anything, the conclusions are even more probative than conclusions based on a smaller scale study. Furthermore, while Applicant argues that the Hu et al. reference contains certain statistical flaws, the instant specification provides no statistical analysis of the data presented in Example 18, which Applicant has relied upon to establish utility for the claimed PRO1268 polypeptides. In addition, the specification of the instant application does not complement the PRO1268 gene expression data with any protein studies. The skilled artisan would not reasonably assume that PRO1268 polypeptide is overexpressed in certain cancer tumors based on the disclosure regarding PCR data without actually testing for PRO1268 polypeptide overexpression.

Applicant submits that Madoz-Gurpide et al. only state that it is unclear how well RNA levels reported correlate with protein levels. Applicant argues that while proteomics is a complementary technology to PCR, this does not mean that proteomic experiments are required in addition to measurements of mRNA levels to determine protein expression. Applicant states that while additional information may be useful in elucidating the detailed biological function of a protein, it is not required to establish utility of a protein as a marker for cancer. Applicant cites Celis et al. (cited by Examiner in the previous Office Action) and indicates that significant correlations between gene and protein expression are most likely to be observed for genes associated with cancer.

Applicant's arguments have been fully considered but are not found to be persuasive. Madoz-Gurpide state that "numerous alterations may occur in proteins that are not reflected in

changes at the RNA level" (p. 53, 2nd full paragraph). Madoz-Gurpide et al. continue to disclose that "[u]nlike PCR that provide one measure of gene expression, namely RNA levels, there is a need to implement protein microarray strategies that address the many different features of proteins including determination of their levels in biological sample..." (p. 53, 3rd full paragraph). Madoz-Gurpide et al. do state that numerous published studies using PCR justify the use of this technology for uncovering patterns of *gene expression*. The reference does not state that the published studies using PCR uncover patterns of *protein expression*. Furthermore, Madoz-Gurpide et al. disclose that most published tumor studies using PCR have either examined a pathologically homogeneous set of tumors to identify clinically relevant subtypes, for example survivors vs. non-survivors, or pathologically distinct subtypes belonging to the same lineage, for example limited stage vs. advanced stage tumors to identify molecular correlates, or tumors of different lineages to identify molecular signatures for each lineage (p. 52, 1st paragraph).

Additionally, although proteomics is a complementary technology to PCR, it is quite clear that the state of the art is such that polypeptide levels cannot be accurately predicted from mRNA levels. Celis et al. emphasize that proteins are frequently the functional molecules and, therefore, the most likely to reflect differences in gene expression (p. 6, bottom of col 1). Celis et al. continue to explain that "[g]enes may be present, they may be mutated, but they are not necessarily transcribed. Some messengers are transcribed but not translated, and the number of mRNA copies does not necessarily reflect the number of functional protein molecules" (p. 6, col 2). As mentioned in the previous Office Action, Madoz-Gurpide et al. teach that there is also intense interest in the scientific field in applying proteomics to disease marker identification and

such approaches include comparative analysis of protein expression in normal and cancer tissues to identify aberrantly expressed proteins that may represent novel markers (p. 54, 2nd full paragraph). Wildsmith et al. also disclose that the gene expression data obtained from a microarray may differ from protein expression data ("Gene Expression Analysis Using Microarrays" Molecular Biology in Cellular Pathology, (2003) England: John Wiley & Sons, p. 283). Thus, the state of the art supports the Examiner's assertion that PCR cannot accurately predict protein levels and that analysis of protein expression is required to identify a protein as a potential marker for cancer.

Applicant asserts at p. 20-24 of the Response of 11 April 2006 that the data of Example 18 clearly establishes the association between PRO1268 and tumor formation and that this provides sufficient evidence to establish a useful and verifiable utility, presumably one of cancer detection or treatment. Applicant submits that it is sufficient to provide a single patentable utility, which has been done by showing that PRO1268 is a diagnostic marker for kidney tumor. Applicant notes that there is no requirement that the specification provide a physiological or biochemical explanation regarding how the claimed polypeptide provides the useful function of being a diagnostic of kidney cancer. Applicants further contend that lack-of-utility rejections are rarely sustained by federal courts, and cite the case of *In re Gazave* (54 C.C.P.A. 1524, 379 F.2d 973, 1967).

Applicant's arguments have been fully considered but are not found to be persuasive. Firstly, it is clear that the In re Gazave case occurred long before the more recent changes in Utility Requirements (Federal Register, 2001, 66(4): 1092-1099). In addition, the examiner in

that case had incorrectly rejected the claims over Utility, when in fact there was ample evidence for a substantial and specific Utility for the claimed isoflavones. Applicants had performed a series of therapeutic experiments in Guinea pigs in which isoflavones were administered and several measurements were taken related to ascorbic acid concentrations and vitamin-P disposition. They also determined the mode of administration for human therapy using isoflavones (e.g. orally, cutaneously, parenterally) as well as the recommended dosages. 35 U.S.C. §101 requires a specific, substantial, and credible utility, or well-established utility for an invention. Such a utility has to be a "real world" context of use which does not require significant further research. In the Gazave case cited by Applicants, most of the evidence and research was fully developed at the time of filing. This is in contrast to a single static measurement in one tissue, in the instant case. In addition, it is not even clear what disease the claimed invention is meant to treat. One cannot be sure that inhibiting the PRO1268 gene will have any negative effect on cancer. Determining a specific disease to be treated by a protein constitutes significant further research and development, which is not acceptable under 35 U.S.C. § 101.

In the instant case, the specification fails to disclose the biological functions, physiological significance, or any specific and substantial utility of the claimed PRO1268 polypeptides. Without such information, how can one in the skilled art use the claimed invention in a meaningful manner? See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

35 U.S.C. § 112, first paragraph (Enablement)

Claims 6-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth for claims 6-17 at p. 6-10 of the previous Office Action (9 January 2006).

Applicant states that a specific and substantial asserted utility has been described above. However, since Applicant has not provided evidence to demonstrate that the PRO1268 polynucleotide and polypeptide have a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention. It is noted that the instant specification is required to teach one skilled in the art how to make and use the claimed polypeptide.

However, even if the claimed invention is eventually deemed to have a credible, specific and substantial asserted utility or a well established utility, claims 6-17 would remain rejected under 35 U.S.C. § 112, first paragraph.

Applicants did not present further arguments related to Enablement of the claimed invention, stating that Enablement in this case is dependent on the Utility of the invention (11 April 2006, p. 26).

Conclusion

No claims are allowable.

This is a continuation of applicant's earlier Application. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds

and art of record in the next Office action if they had been entered in the earlier application.

Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case.

See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
17 July 2006

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER